I. Formal Matters

Applicants have added a "Brief Description of the Figures" section at page 3 of the specification and request that the objection to the specification be withdrawn.

Applicants have submitted an abstract on a separate sheet of paper to comply with the requirements of 37 CFR 1.72(b).

Applicants have requested a certified copy of the priority document, but have not yet received it. It will be filed as soon as it is received.

II. Rejections Under 35 U.S.C. § 112, First Paragraph

A. The Office has rejected claims 1-10 as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and use the invention. The Office contends that "there is insufficient guidance and direction in the specification on how to make and use said antibody."

Applicants respectfully traverse this rejection. The claimed invention relates to (1) monoclonal antibodies that bind the beta 2 chain of the IL-12 receptor on the surface of human T lymphocytes and prevent tyrosine phosphorylation of STAT4, (2) monoclonal antibodies that bind the beta 2 chain of the IL-12 receptor on the surface of human T lymphocytes and prevent dimerization of the beta 2 chain of the receptor with the beta 1 chain, and (3) monoclonal antibodies that do both. As stated at page 3 of the specification, IL-12 exerts its effects through binding to the high affinity receptor IL-12R composed of a beta1 and a beta 2 chain. The beta 2 chain is responsible for signal transduction and this signal involves the tyrosine phosphorylation of STAT4 (See page 5, lines 19-29). It was also known that in order for the receptor to bind IL-12 with high affinity it must undergo a dimerization of the beta 1 and beta 2 chains. By blocking

this dimerization, IL-12 will not be able to bind and induc the synthesis of IFN-gamma by T-cells. Thus, a skilled artisan would recognize that a monoclonal antibody binding to the beta 2 chain could block dimerization of the two chains of the IL-12R, prevent phosphorylation of STAT4, or both depending on the binding site of the antibody.

Example 3 of the present specification describes the technique used for generating anti-IL12R beta 2 chain monoclonal antibodies. At the time the present invention was made, monoclonal antibody techniques were well known and routine in nature. Generating a monoclonal antibody to the IL12R beta 2 chain was well within the skill of an artisan given the description in example 3 and the state of the monoclonal antibody art at the time the invention made. Example 5 at pages 12-13 clearly teaches one skilled in the art how to identify monoclonal antibodies that prevent the tyrosine phosphorylation of STAT4. Page 6 of the specification provides a simple routine test for determining whether the monoclonal antibody blocks the dimerization of the beta 1 and beta 2 chains of the IL-12R. Given the level of skill in the art and the clear guidance in the specification, it would not have required undue experimentation for the skilled artisan to make and use the monoclonal antibodies of the claimed invention.

The Office has stated that U.S. Patent No. 5,831,007 teaches "that no neutralizing monoclonal antibodies to the IL-12 receptor are currently available." This may have been true in 1993 when the application for that patent was filed. At that time, only the beta 1 chain was known, therefore one could not have made an antibody to the beta 2 chain. However, at the time of filing of the present application, the beta 2 chain had been identified and it was known that it was in fact the beta 2 chain that was responsible for signal transduction. Therefore, the teachings of the '007 patent have no

bearing on the sufficiency of the present disclosure to teach a skilled artisan how to make and use neutralizing antibodies to the beta 2 chain of the IL-12 receptor.

In view of these remarks, Applicants submit that the specification sufficiently enables the full breadth of the claims and it would not have required a skilled artisan undue experimentation to make and use the monoclonal antibodies of the claimed invention. Therefore, the rejection should be withdrawn. Although claims 4-10 have been cancelled, rendering the rejection as to those claims moot, Applicants submit that the rejection should not apply to new claims 11-22 in view of the arguments presented.

B. The Office has rejected claims 1-10 as containing subject matter which was not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention at the time the application was filed.

Applicants respectfully traverse this rejection. As stated above, the specification provides clear guidance as to how to generate antibodies to the beta 2 chain of the IL-12R and how to characterize the antibodies generated to determine if the antibody exhibits the required elements of the claims. The Written Description Guidelines, specifically Example 16 (Applicants have attached this Example for the Examiner's convenience), state that antibody technology is a well developed and mature field, the making of antibodies is a routine, art recognized method when, as in this case the antigen is well characterized, and that the level of skill in this mature technology is high and advanced. Moreover, one of skill in the art would have recognized that the spectrum of antibodies which bind to IL-12R beta 2 chain having the functional characteristics claimed are implicitly disclosed as a result of the isolation of the antigen. Thus, th rejection of claims 1-3 for lack of written description is inappropriate and should be withdrawn.

In addition, in view of the fact that the monoclonal antibodies of claims 1-3 are novel and non-obvious, any compound added to such compositions as those claimed in claims 11-18 are by definition novel and nonobvious by virtue of the monoclonal antibody. However, for purposes of written description, the new claims specifically define the second monoclonal antibody as being one that binds to a costimulatory molecule on T-cells or antigen presenting cells. This is easily tested and sufficiently described. The specification at page 7 defines "autoantigen" as being "a human protein that is recognized by autologous T-cells, resulting in self-tissue destruction in autoimmune disease patients." Modified forms of these autoantigens are described as having amino acid substitutions and may also be fragments of the native form or the modified form. Therefore, a skilled artisan would readily recognize what autoantigens and second monoclonal antibodies are encompassed by the claims.

In view of these remarks, Applicants request that the rejection be withdrawn. Although claims 4-10 have been cancelled, rendering the rejection as to those claims moot, Applicants submit that the rejection should not apply to new claims 11-22 in view of the arguments presented.

Conclusion

In view of the foregoing amendments and remarks, Applicants submit that the application is condition for allowance and request a timely notice.

Respectfully Submitted,

Dated: July 12, 2002.

BY: Cheryl A. Liljestrand
Cheryl A. Liljestrand
Reg. No. 45,275

Example 16: Antibodies

Specification: The specification teaches that antigen X has been isolated and is useful for detection of HIV infections. The specification teaches antigen X as purified by gel filtration and provides characterization of the antigen as having a molecular weight of 55 KD. The specification also provides a clear protocol by which antigen X was isolated. The specification contemplates but does not teach in an example antibodies which specifically bind to antigen X and asserts that these antibodies can be used in immunoassays to detect HIV. The general knowledge in the art is such that antibodies are structurally well characterized. It is well known that all mammals produce antibodies and they exist in five isotypes, IgM, IgG, IgD, IgA and IgE. Antibodies contain an effector portion which is the constant region and a variable region that contains the antigen binding sites in the form of complementarity determining regions and the framework regions. The sequences of constant regions as well as the variable regions subgroups (framework regions) from a variety of species are known and published in the art. It is also well known that antibodies can be made against virtually any protein.

Claim: An isolated antibody capable of binding to antigen X.

Analysis:

A review of the full content of the specification indicates that antibodies which bind to antigen X are essential to the operation of the claimed invention. The level of skill and knowledge in the art of antibodies at the time of filing was such that production of antibodies against a well-

characterized antigen was conventional. This is a mature technology where the level of skill is high and advanced.

The claim is directed to any antibody which is capable of binding to antigen X.

A search of the prior art indicates that antigen X is novel and unobvious.

Considering the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized that the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X.

Conclusion: The disclosure meets the requirement under 35 USC 112 first paragraph as providing an adequate written description of the claimed invention.